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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/077,615 10/23/98 ARGUELLO

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EXAMINER

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ART UNIT	PAPER NUMBER

1655
DATE MAILED:

03/27/01

19

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

<p align="center">Office Action Summary</p>	<p>Application No.</p> <p>09/077,615</p>	<p>Applicant(s)</p> <p>ARGUELLO ET AL.</p>	
	<p>Examiner</p> <p>Juliet C. Einsmann</p>	<p>Art Unit</p> <p>1655</p>	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 December 2000.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 39-54 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 39-54 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- | | |
|---|---|
| 15) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 18) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 16) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 19) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 17) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 20) <input checked="" type="checkbox"/> Other: <i>CRF Problem Report paper no. 18</i> |

DETAILED ACTION

1. This action is written in response applicant's correspondence submitted December 22, 2000, paper number 14. All previously pending claims were cancelled, and claims 39-54 were added. Claims 39-54 are pending. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. **This action is FINAL.**

Specification

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). The CRF submitted with the response to the Office Action had errors which prevented it from being entered into the database (see attached CRF Problem Report). Further, there are sequences in the specification which are not identified with a proper sequence identifier (see, for example, p. 35). Applicant is required to submit a new CRF, an amendment directing the insertion of the SEQ ID NOs into the appropriate pages of the specification and a letter stating that the content of the paper and computer readable copies are the same.

3. The disclosure is objected to because of the following informalities:

The specification does not contain a description of the drawings as set out in 37 CFR 1.74.

Page 1 of the specification is cut off at the bottom. A substitute is required.

Appropriate correction is required.

**NEW GROUNDS OF REJECTION AND OBJECTION NECESSITATED BY
APPLICANT'S AMENDMENT OF THE CLAIMS**

Claim Objections

4. Claim 43 is objected to because of the following informalities: The claim is confusing because of the use of the (a) and (b) to indicate both the steps of the claim (lines 2 and 5 of the claims) and the limitations on the control duplexes (lines 6 and 8 of the claim). Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. Claims 39-40 and 42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 39-40, 42 are indefinite over the recitation of "run under a heated condition" because the metes and bounds of this limitation are unclear. To some extent, every condition is heated, and it is not clear how this inclusion is meant to limit the instant claims.

Claims 49-52 are indefinite over the recitation of "have corresponding alleles" because this term is unclear. It is not clear what the meaning of corresponding alleles is.

Claim 51 is indefinite because its relationship to claim 50, from which it depends is not clear. It is not clear how the paternity testing of claim 51 relate to the tissue donor and recipient of claim 50.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

Art Unit: 1655

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 39-45 and 48 are rejected under 35 U.S.C. 102(b) as being anticipated by Zimmerman *et al.* (Nucleic Acids Research, 1993, Vol. 21, No. 19, 4541-4547).

Zimmerman *et al.* teach a method for identifying an HLA gene comprising:

(a) contacting the DNA molecule with a labeled reference DNA strand under conditions such that the reference strand hybridizes to a complementary strand of the DNA molecule so as to form a test duplex (p. 4542, heading “DHDA”);

(b) running the test duplex and one or more control duplexes in a gel by electrophoresis, wherein the gel contains urea, a denaturing agent, and the gel is heated to between 40° C and 45° C (p. 4542, heading “DHDA”); and

(c) comparing the position of the test duplex on the gel with the position of the control duplexes (p. 4543 and Fig. 2 and Fig. 3).

(d) repeating steps (a)-(c) one or more times wherein a different allelic strand is used in each repeat to identify the DNA molecule (see figure description for figure 3, the test was run with both DQA1*0102 and DQA1*0501 as the reference probe).

In the method taught by Zimmerman *et al.* the control duplexes are duplexes which have graded mobilities and which are run in a different lane on the gel to the test duplex. Zimmerman *et al.* specifically teach that “every DQA1 allele, with the exception of DQA1*0601 can be distinguished by the unique mobility of one or both of its HD bands.” With regard to the limitation of claim 47, the comparison of the test duplexes in figure 3 with the reference gel in

Art Unit: 1655

figure 3 is considered to be a comparison of the position of the test duplex with a database of values.

8. Claim 49 is rejected under 35 U.S.C. 102(b) as being anticipated by Wu (US 5387505).

Wu teaches a method for determining whether two individuals have corresponding alleles, which method comprises:

(a) amplifying the alleles of a first individual employing a pair of primers in which one of the primers has a ligand molecule attached (Col. 9, lines 21-30, 47-55);

(b) contacting the amplified mixture of double stranded DNA molecules with an receptor on solid support under conditions such that the biotin binds the avidin (Col. 9, lines 56-63);

(c) separating the mixture of double-stranded DNA molecules into single-strands and removing the strands that are not bound to the support by the ligand (Col. 10, lines 1-8);

(d) recovering the remaining strands from the solid support (Col. 10, lines 9-17);

(e) mixing the recovered strands with a complementary strand the alleles of the second individual so as to form duplexes (Col. 11, lines 34-40); and

(f) separating the duplexes (Col. 11, lines 47-49); and

(g) analyzing the test duplexes to determine whether the alleles of the gene from the first individual correspond with the alleles of the second individual (Col. 11, lines 50-60).

The probe used by Lu is a probe to an HLA allele, and therefore, it is inherently an allele from a second individual.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

Art Unit: 1655

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claim 46 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zimmerman *et al.*

Zimmerman *et al.* teach a method for identifying an HLA gene comprising:

(a) contacting the DNA molecule with a labeled reference DNA strand under conditions such that the reference strand hybridizes to a complementary strand of the DNA molecule so as to form a test duplex (p. 4542, heading "DHDA");

(b) running the test duplex and one or more control duplexes in a gel by electrophoresis, wherein the gel contains urea, a denaturing agent, and the gel is heated to between 40° C and 45° C (p. 4542, heading "DHDA"); and

(c) comparing the position of the test duplex on the gel with the position of the control duplexes (p. 4543 and Fig. 2 and Fig. 3).

(d) repeating steps (a)-(c) one or more times wherein a different allelic strand is used in each repeat to identify the DNA molecule (see figure description for figure 3, the test was run with both DQA1*0102 and DQA1*0501 as the reference probe).

In the method taught by Zimmerman *et al.* the control duplexes are duplexes which have graded mobilities and which are run in a different lane on the gel to the test duplex. Zimmerman *et al.* specifically teach that "every DQA1 allele, with the exception of DQA1*0601 can be distinguished by the unique mobility of one or both of its HD bands."

Zimmerman *et al.* do not exemplify this method wherein the labeled reference DNA strand is labeled with a compound that allows an enzyme molecule to be attached to the reference DNA strand. However, Zimmerman does expressly teach that "DHDA can be easily

Art Unit: 1655

converted to non-radioactive reagents through strategic use of biotinylated primers and strepavidin linked enzyme detection (p. 4545, Col. 2)."

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have used biotin as the label in the methods taught by Zimmerman *et al.* The ordinary practitioner would have been motivated by the teachings of Zimmerman *et al.* to make such a change to the methods since Zimmerman *et al.* suggest the substitution and teach that non-radioactive detection methodologies are advantageous (p. 4545).

11. Claims 50-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wu in view of Clay *et al.* (The Lancet, 1991, Vol. 337, p. 1049-1052).

Wu teaches a method for determining whether two individuals have corresponding alleles, which method comprises:

(a) amplifying the alleles of a first individual employing a pair of primers in which one of the primers has a ligand molecule attached (Col. 9, lines 21-30, 47-55);

(b) contacting the amplified mixture of double stranded DNA molecules with an receptor on solid support under conditions such that the biotin binds the avidin (Col. 9, lines 56-63);

(c) separating the mixture of double-stranded DNA molecules into single-strands and removing the strands that are not bound to the support by the ligand (Col. 10, lines 1-8);

(d) recovering the remaining strands from the solid support (Col. 10, lines 9-17);

(e) mixing the recovered strands with a complementary strand the alleles of the second individual so as to form duplexes (Col. 11, lines 34-40); and

(f) separating the duplexes (Col. 11, lines 47-49); and

(g) analyzing the test duplexes to determine whether the alleles of the gene from the first individual correspond with the alleles of the second individual (Col. 11, lines 50-60).

The probe used by Wu is a probe to an HLA allele, and therefore, it is inherently an allele from a second individual. Furthermore, Wu teaches that hybridization assays are used in methods for the determination of paternity and immigration screening (Col. 1, lines 38-39).

Wu does not teach a method in which the first individual and second individual are selected from the group consisting of a prospective tissue donor and a prospective tissue recipient.

Clay *et al.* teach methods for HLA matching of unrelated marrow donors which in which the DNA of prospective donors is directly hybridized with that of recipients during a PCR reaction. The heteroduplexes formed are run on a test gel and analyzed to determine the alleles of the samples. Furthermore, Clay *et al.* a step in which test duplexes are further analyzed using sequence specific oligonucleotide analysis to confirm the determination of the allele (p. 1051, Col. 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have combined the methods of Wu with those taught by Clay *et al.* because Clay *et al.* teach that the heteroduplexes formed by the hybridization of donor and recipient DNA are useful for typing HLA alleles, and Wu teach that their method is also useful for HLA allele typing.

12. Claim 54 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wu in view of Clay *et al.* as applied to claims 50-53 above, and further in view of Gao *et al.* (Human Immunology, 41, 267-279 (1994)).

Art Unit: 1655

The teachings of Wu in view of Clay *et al.* are applied to these claims as presented in the rejection of claims 50-53. Wu in view of Clay *et al.* do not teach the use of this method for typing of HLA Class I alleles.

Gao *et al.* teach that typing HLA Class I alleles "DNA typing should be practiced in donor-recipient matching, at least for those serologically undetectable class I subtypes (p. 278, Col. 1)." Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have used the method taught by Wu in view of Clay *et al.* for typing of HLA Class I alleles in addition to the Class II alleles already taught for typing in Wu and Clay *et al.*, since the combined teachings of Wu in view of Clay *et al.* provide a rapid and effective methodology for typing these medically important alleles, and Gao *et al.* teach that HLA Class I alleles are important in transplantation.


Conclusion

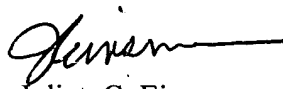
13. No claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Einsmann whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.


W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600


Juliet C. Einsmann
Examiner
Art Unit 1655

March 22, 2001

3/23/01